REMARKS

Claims 1-8, 11-13, 15-24, 29-30, 32-38, 40-48, 50-53, 55-57, 62-63, 65-67, 69-71, 76-80, 82-85 and 90 are pending and claims 1-8, 11-13, 15-19, 21-23, 25, 29-30, 32-38, 40-43, 45-48, 50, 53, 55-57, 62-63, 65-67, 71 and 76-78 have been examined on the merits. The pending claims are cancelled hereinabove and new claims 91-107 are added. Support for the new claims can be found in the specification from page 5, line 30 to page 6, line 7, and lines 14-21, on page 7 lines 9-11, in figures 2 and 4 and generally in the subject matter of cancelled claims 1-8, 11-13, 15-19, 21-23, 25, 29-30, 32-38, 40-43, 45-48, 50, 53, 55-57, 62-63, 65-67, 71 and 76-78. No new matter has been added.

In the Office Action, the claims are restricted to the following four inventions:

1. Group I, claims 1-8, 11-13, 15-19, 21-23, 25, 29-30, 32-38, 40-43, 45-48, 50, 53, 55-57, 62-63, 65-67, 71 and 76-78 drawn to the first appearing technical feature the water binding covalently reactive polypeptide antigen binding analog of formula I as set forth in claim 2, all the method of using;
2. Group II, claims 51 and 52, drawn to the second appearing technical feature a catalytic antibody produced by a particular process;
3. Group III, claims 69-70, drawn to methods of using the second technical feature of the antibody of Group II claims; and
4. Group IV, claims 79-80, 82-85 and 90, drawn to methods of use of any pCRA and do not recite the technical feature of Group II claims.

The Examiner has requested that the specification be amended to comply with the Sequence Rules and has notified Applicants that the references listed in the specification have

not been considered unless they have been cited by the Examiner on form PTO-892 or have been provided by Applicants in a 1449.

Moreover, the Examiner has rejected the claims as follows:

5. Claims 1-8, 11-13, 15-19, 21-23, 25, 29-30, 32-38, 40-43, 45-48, 50, 53, 55, 56-57, 62-63, 65-67, 71 and 76-78 are rejected under 35 U.C.C. § 112, ¶ 1, for allegedly failing to comply with the written description requirement;

6. Claims 34-36 are rejected under 35 U.S.C. § 112, ¶ 1, for allegedly failing to comply with the enablement requirement;

7. Claims 76-78 are rejected under 35 U.S.C. § 112, ¶ 1, for allegedly failing to comply with the enablement requirement;

8. Claims 1-8, 11-13, 15-19, 21-23, 25, 29-30, 32-38, 40-43, 45-48, 50, 53, 55-57, 62-63, 65-67 and 71 are rejected under 35 U.S.C. § 112, ¶ 2, for allegedly being indefinite;

9. Claims 12-19, 38, 41-43, 45-48, 50, 53, 56-58, 62-63, 65, 67 and 76-78 are rejected under 35 U.S.C. § 112, ¶ 4, for allegedly being of improper dependent form; and

10. Claims 38, 45-48, 50, 53, 55-57, 62-63 and 65-66 are rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Paul et al. (U.S. Patent No. 6,235,714, hereinafter "Paul").

Applicants respectfully traverse these rejections.

Restriction Requirement

Applicants elect to prosecute the Group I claims directed to the first appearing technical feature, the method of using water binding covalently reactive polypeptide antigen binding analogs of formula (I).

However, claims 1-8, 11-13, 15-19, 21-23, 25, 29-30, 32-38, 40-43, 45-48, 50, 53, 55-57, 62-63, 65-67, 71 and 76-78 are cancelled hereinabove and replaced with new claims 91-107 which are drawn to the generally same subject matter of the cancelled claims.

Sequence Requirement

In the Office Action, the Examiner has directed Applicants to amend the specification to place the relevant sequence identifier after the appropriate sequences, for example on page 8 and 36. For the following reasons, it is respectfully submitted that the specification fully complies with the Sequence Rules.

Under 37 C.F.R. § 1.821 (a), nucleotide and/or amino acid sequences are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotide.

The sequences pointed out by the Examiner, i.e., Pro-Phe-Arg-MCA et sequitur (*e.g.*, starting at page 7, line 33), are not unbranched sequences of four or more amino acids. As described in the specification on page 46, line 30, "MCA" is the abbreviation of "methylcoumarinamide" which is not an amino acid. Therefore, the various sequences ending with MCA are only three amino acids long and do not need to be identified by a specific sequence identifier. Moreover, Applicants point out to the Examiner the amendment to the specification filed on July 30, 2009, in which the specification has been amended on page 36, line 32 and on page 52, line 27 to comply with Sequence Rules. Accordingly, in light of the

above, it is respectfully submitted that the application is fully compliant with the Sequence Rules.

Information Disclosure Statement

Under 37 C.F.R. § 1.56, each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability. Applicants have complied with the duty to disclose by filing the Information Disclosure Statement of February 6, 2007. No other information material to patentability of the presently claimed invention is known at this time.

Rejection under 35 U.S.C. § 112, ¶ 1: Written Description

New claim 91 is directed to a method for obtaining covalent or catalytic antibodies from organisms or transgenic mice using a covalently reactive polypeptide antigen analogue (pCRA) of formula L-E in which L is a ligand that binds noncovalently to a nucleophile receptor Nu and E is an electrophilic group conjugated to a side chain functional group of L having the formula Y-Y'-Y", wherein Y" is an atom, covalent bond or linker, Y' is an atom, bond or chemical group that connects Y and L or Y"; and Y is a covalently reactive electrophilic group that reacts specifically with an antibody that binds to L (*e.g.*, from page 5, line 30 to page 6, line 7, and lines 14-21, page 7 lines 9-11, figures 2 and 4).

In the Office Action the Examiner has taken the position that although the disclosure would put the skilled artisan in possession of different electrophilic groups of Figure 5, the level of skill and knowledge in the art is such that one of ordinary skill would not be able to identify without further testing, which of those combinations with all the other plethora of elements would have the necessary functional activities (*e.g.*, Office Action, pages 5-6).

Applicants respectfully disagree with these comments.

As an initial matter a description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). Thus, it is the Examiner that has the initial burden of presenting, by a preponderance of the evidence, why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257, 263 191 USPQ 90, 97 (CCPA 1976). Applicants respectfully submit that the Examiner has not met his burden. According to the Examiner, the specification lacks written description of a representative number of pCRA variants to support the genus claimed and that therefore those skilled in the art would not conclude that Applicants were in possession of the claimed genus (*e.g.*, page 6, lines 1-4 of the Office Action).

However, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, by reduction to drawings, by disclosure of relevant, identifying characteristics, by functional characteristics coupled with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. *Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398,1406 (Fed. Cir. 1997).

Applicants have previously indicated that the specification discloses the structures of electrophiles (*e.g.*, Figures 5A-5C), and has submitted that the pCRAs' structures represent a broad genus unified by the common feature of covalent reactivity of the electrophile incorporated in the pCRAs with nucleophilic antibodies (*e.g.*, page 21 of the response submitted

on May 12, 2010). Moreover, Applicants have also indicated that the specification discloses structural examples of pCRAs encompassing the entire genus in Examples I, III, VI, VIII, X and XI.

Accordingly, the specification discloses how to synthesize the pCRAs by using the described electrophiles and linkers to bond the appropriate functional groups in the peptide or protein antigenic sequence and how to screen and select for the produced antibodies.

Further, it is well known in the art how to immunize an organism and that near homologues or analogs of a chemical structure are likely to be functionally similar, if not identical.

Thus, because a "representative number" of species is an inverse function of the skill and knowledge in the art, Applicants respectfully submit that the specification describes a sufficient and representative number of species and identifies their structural characteristics coupled with their functions.

One of ordinary skill in the art would be capable to design alternative linkers for the instant pCRAs, based on the particular side chain functional groups of L and the particular electrophile or Y'-Y without undue experimentation and with a reasonable expectation of success. Moreover, one of ordinary skill would also be capable to design a suitable electrophile given the general knowledge in the art and the disclosure of many electrophilic structures in the specification.

Because the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces, Applicants respectfully submit that the specification has satisfied the written description requirement for the claimed genus.

On the other hand, the Examiner has not met her burden. In light of the above, the Examiner's statement that "the specification lacks the written description of a representative number of pCRA variants to support the genus claimed" is not enough to establish, by a preponderance of the evidence, why a person skilled in the art would not be able to recognize in an applicant's disclosure a description of the invention defined by the claims.

Accordingly, for all of the reasons set forth above, it is respectfully submitted that the claims comply with the written description requirement and Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 112, ¶ 1: Enablement

Claims 34-36 and 76-78 are cancelled hereinabove rendering their rejection moot. Accordingly, withdrawal of the claim rejection under 35 U.S.C. § 112, ¶ 1, for failing to comply with the enablement requirement is respectfully requested.

Rejection under 35 U.S.C. § 112, ¶ 2

Claims 1-8, 11-13, 15-19, 21-23, 25, 29-30, 32-38, 40-43, 45-48, 50, 53, 55-57, 62-63, 65-67 and 71 are cancelled hereinabove rendering this rejection moot.

As supported in the specification on page 22, lines 30, 32 and on figure 2, specification the pCRA structure presently claimed is based on the split site model of covalent/catalytic antibodies in which the antibody paratope and nucleophilic regions are treated as two distinct subsites.

Accordingly, it is respectfully submitted that the claims are not indefinite and withdrawal of the rejection under 35 U.S.C. § 112, ¶ 2 is respectfully requested.

Rejection under 35 U.S.C. § 112, ¶ 4

Claims 12-19, 38, 41-43, 45-48, 50, 53, 56-58, 62-63, 67 and 76-78 are cancelled hereinabove rendering their rejection moot. Accordingly Applicants respectfully request that the rejection under 35 U.S.C. § 112, ¶ 4 be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 102(b)

As discussed above, the presently claimed invention is directed to a method of obtaining covalent or catalytic antibodies from organisms, such as those with an autoimmune or alloimmune disease or without known diseases or transgenic mice expressing human antibody genes using the pCRA of formula L-E wherein L is a ligand that binds noncovalently to a nucleophilic receptor Nu and E is an electrophilic group conjugated to a side chain functional group of L having the formula

Y-Y'-Y"-

wherein Y" is an atom, covalent bond or linker, Y' is an atom, bond or chemical group that connects Y and L or Y" and Y is a covalently reactive electrophilic group that reacts specifically with an antibody that binds to L (*e.g.*, from page 5, line 30 to page 6, line 7, and lines 14-21, page 7 lines 9-11 and figures 2 and 4). In other words, the presently claimed invention requires that Y, the covalently reactive electrophilic group reacting specifically with the antibody that binds to L, be covalently linked through Y' and Y" to a side chain functional group of L.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. *Verdeegal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Paul is not an anticipatory reference for the presently claimed subject matter. Paul describes covalently reactive antigen analogs of structure X_1-Y-E-X_2, wherein E is an

electrophilic reaction center designed to react covalently with nucleophilic side chains of certain amino acids, Y is a basic residue (Arg, or Lys) at the P1 position (first amino acid on the N-terminal side of the reaction center) and X_1 and X_2 comprise three to ten flanking amino acids on the N and C terminal sides of the reaction center (*e.g.*, col. 3, lines 28-36 and Figures 4 and 15-17).

Accordingly, Paul does not disclose the pCRA presently claimed. As an initial matter Paul does not disclosed the presence of Y", which is an atom, covalent bond or linker connecting the electrophilic group to the peptide but only discloses that Y is directly linked to the N terminal of X_1. Second, the electrophilic group is flanked by two chains (X_1 and X_2) constituted by three to ten aminoacids, and third, Paul does not discloses that the electrophilic group is linked to an amino acid's side chain functional group.

Thus, Paul does not disclose each and every element as set forth in the claims and therefore cannot anticipate the presently claimed subject matter.

Therefore, for all of the reasons set forth above, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be reconsidered and withdraw.

Conclusion

This response is being filed with a petition for a two month extension of time. Thus, no additional fees are believed to be due. If, on the other hand, it is determined that further fees are necessary or any overpayment has been made, the Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as

incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

An early and favorable action on the merits is earnestly solicited

Respectfully submitted

Date: December 16, 2011

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